Overview – Chemical and Scoring Ranking Assessment Model

SCRAM: A Scoring and Ranking System for Persistent, Bioaccumulative, and Toxic Substances for the North American Great Lakes *

Part I: Structure of the Scoring and Ranking System *(ESPR No. 1, 2000)* **DOI: http://dx.doi.org/10.1065/espr199910.009**
Part II: Bioaccumulation Potential and Persistence *(ESPR No. 2, 2000)* **DOI: http://dx.doi.org/10.1065/espr199910.010**
Part III: Acute and Subchronic or Chronic Toxicity *(ESPR No. 3, 2000)* **DOI: http://dx.doi.org/10.1065/espr199910.011**
Part IV: Results from Representative Chemicals, Sensitivity Analysis, and Discriminatory Power *(ESPR No. 4, 2000)* **DOI: http://dx.doi.org/10.1065/espr199910.012**

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Part I: Structure of the Scoring and Ranking System

Hundreds of chemical contaminants have been identified in the Great Lakes System of North America. Depending on the agency or organization, various subset lists of these contaminants have been identified as chemicals of potential concern. However, there is no agreement on the method that should be used to make management decisions. Except for consensus on approximately 40 chemicals that most North American agencies agree can cause deleterious effects if released into the environment, no agreement has been reached regarding the priority that contaminants should receive for further action. That leaves hundreds of chemicals that have been, are being, or potentially could be released into the environment that have not been evaluated yet. A profile for potential chemicals of concern is generally thought to include persistence in the environment, potential to bioaccumulate, and ability to cause toxic effects at environmentally relevant concentrations. Except for the International Joint Commission's definition of persistence (> 8 weeks residence time in air, water, soil or sediment), there is little concurrence about what defines these characteristics. For instance, the State of Michigan currently has no established definitions or profiles of persistent, bioaccumulative, toxic substances. Furthermore, there is no standard process to rank chemicals relative to these characteristics. The Chemical Scoring and Ranking Assessment Model (SCRAM) has been developed to provide a process to rank-order chemicals based on these characteristics. The SCRAM system was developed primarily for use in the Great Lakes region of North America and particularly in Michigan, but it is not site-specific. Use of this system may assist in pollution prevention activities and other future chemical control efforts, allowing attention to be focused first on those chemicals likely to present the greatest hazard.

Part II: Bioaccumulation Potential and Persistence

Part I of this series introduced SCRAM, a chemical scoring and ranking system for contaminants of the North American Great Lakes. Here, in **Part II**, scoring of the bioaccumulation potential and persistence of chemicals is discussed, including acceptable types of data, specific scoring instructions, and the basis for criteria and scores for these categories of the system. Difficulties encountered during the process of determining which types of data adequately represent the properties of interest are discussed. Also, justification is given for an emphasis on scoring on the basis of persistence.

Part III: Acute and Subchronic or Chronic Toxicity

In **Part II**, scoring of the potential for a chemical to persist in the environment and bioaccumulate was described. In **Part III**, scoring of chemical toxicity is discussed, including definitions and descriptions of effects that are scored, specific scoring instructions, the basis for the criteria and scores, and specific conditions or concerns regarding the types of data used for scoring. A score for each chemical screened is determined from available test data from acute or subchronic and chronic toxicity tests conducted on aquatic and terrestrial organisms. Subchronic and chronic human health effects, including carcinogenicity, are also considered. Part IV includes an evaluation of the performance of the scoring and ranking system.

Part IV: Results from Representative Chemicals, Sensitivity Analysis, and Discriminatory Power

The Chemical Scoring and Ranking Assessment Model (SCRAM) has been described in **Parts I-III** of this series. SCRAM is a chemical scoring and ranking (CSR) system that scores chemicals on the basis of bioaccumulation potential, environmental persistence, and toxicity. **Part IV** describes various tests and descriptions of the performance of this system. A group of 21 representative chemicals was chosen and scored to test the system. For those chemicals, the percentages of the scores associated with fate-related properties and associated with data uncertainty were determined. The scoring of four of these chemicals is described in greater detail, and the suitability of the scores is discussed. An analysis of the sensitivity of the system to incomplete data sets is presented. And finally, the discriminatory power of the system is described.

* The scoring and ranking system in the form of a Lotus 123[97] spreadsheet and a description of its use are available on the Internet at http://www.epa.gov/toxteam/pbtrept/

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Part I. Structure of the Scoring and Ranking System

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Abstract. Hundreds of chemical contaminants have been identified in the Great Lakes System of North America. Depending on the agency or organization, various subset lists of these contaminants have been identified as chemicals of potential concern. However, there is no agreement on the method that should be used to make management decisions. Except for consensus on approximately 40 chemicals that most North American agencies agree can cause deleterious effects if released into the environment, no agreement has been reached regarding the priority that contaminants should receive for further action. That leaves hundreds of chemicals that have been, are being, or potentially could be released into the environment that have not been evaluated yet. A profile for potential chemicals of concern is generally thought to include persistence in the environment, potential to bioaccumulate, and ability to cause toxic effects at environmentally relevant concentrations. Except for the International Joint Commission's definition of persistence (> 8 weeks residence time in air, water, soil or sediment), there is little concurrence about what defines these characteristics. For instance, the State of Michigan currently has no established definitions or profiles of persistent, bioaccumulative, toxic substances. Furthermore, there is no standard process to rank chemicals relative to these characteristics. The Chemical Scoring and Ranking Assessment Model (SCRAM) has been developed to provide a process to rank-order chemicals based on these characteristics. The SCRAM system was developed primarily for use in the Great Lakes region of North America and particularly in Michigan, but it is not site-specific. Use of this system may assist in pollution prevention activities and other future chemical control efforts, allowing attention to be focused first on those chemicals likely to present the greatest hazard.

Keywords: Acute toxicity; bioaccumulation; chemical scoring and ranking; chronic toxicity; hazard; North American Great Lakes; persistence; priority pollutants; SCRAM (Chemical Scoring and Ranking Assessment Model); uncertainty; water pollution

1 Introduction

It has been estimated that there are approximately 100,000 chemicals in commercial use, and new chemicals are being developed continually. Of those currently in commercial use, approximately 40,000 are used in the Great Lakes Basin. The U.S. Environmental Protection Agency, Office of Pollution Prevention and Toxics (OPPT), receives approximately 2,300 new submittals each year (Zeeman et al., 1995). Simple scoring and ranking criteria have been used in selecting chemicals to be regulated (MDNR, 1987; OMOE, 1990; Meek, 1996; Hertel, 1996; Hansen, 1995; Klöpffer, 1994a,b,c,d; Anon., 1995) or even sunsetted from use (Foran and Glenn, 1993).

A number of schemes have been suggested to screen for the potential of chemicals to cause adverse effects once released into the environment (Swanson and Socha, 1997). The University of Tennessee Center for Clean Products and Clean Technologies identified 147 different scoring and ranking systems and described and critically reviewed 51 of those systems (Davis et al., 1994). These have also been reviewed, compared, contrasted, and evaluated in a workshop conducted by the Society of Environmental Toxicology and Chemistry, or SETAC (Swanson and Socha, 1997). The experts convened at the SETAC meeting made suggestions on the preferred methods of estimating, aggregating, and weighting parameters. While the various scoring and ranking methods vary in the parameters used or in methods of estimation

* The scoring and ranking system in the form of a Lotus 123[97] spreadsheet and a description of its use are available on the Internet at http://www.epa.gov/toxteam/pbtrept/

or aggregation of the parameters within the system, they all function in a similar manner. All of the scoring systems attempt to prioritize for research activities or management decisions the relative potential of chemicals to cause adverse effects based on exposure and effects profiles (HERTEL, 1996; MEEK, 1996; SMRCHEK and ZEEMAN, 1997; SWANSON et al., 1997). The parameters used, either measured or modeled, are estimators or surrogates for the potential for exposure and hazard. In general, estimates of persistence, bioaccumulation, and toxicity are the main parameters used (SWANSON and SOCHA, 1997). In addition to the parameters that describe the environmental fate and toxicological profiles, information on the amount of chemical manufactured or used and the types of uses can also be considered. These ancillary pieces of information can be used in a tiered testing protocol to identify potential candidates for further review or testing. However, this should be done with caution, since some of the most problematical compounds of the past 20 years, the polychlorinated dibenzo-*p*-dioxins (PCDD) and polychlorinated dibenzofurans (PCDF), were neither manufactured for a purpose nor released in quantities that would have been predicted to have the resulting environmental effects.

The Scoring and Ranking Assessment Model (SCRAM) was developed to serve as an analytical tool in chemical scoring and ranking. This simple spreadsheet scoring and ranking system allows risk assessors and managers to calculate an index that is based on the potential exposure and toxicity of chemicals and aids in determining the sufficiency of available data. In many cases, little empirical information is available about the fate, exposure or toxicity of a chemical. Estimates of key parameters that control these properties can be determined, however, with quantitative structure-activity relationships (QSARs) (HERMENS et al., 1985). These statistical relationships often are quite powerful, but there is still a great deal of uncertainty in the exposure or toxicity profiles based on these incomplete data sets (TOSATO et al., 1991; FIEDLER et al., 1990). None of the previously developed scoring and ranking systems have taken this uncertainty into account. SCRAM is unique in its treatment of chemicals for which data are lacking. If few data are available for a chemical, instead of ignoring the chemical, the system flags it as one for which there is a great deal of uncertainty. Thus, chemicals can become candidates for special attention based on inherent chemical characteristics, lack of information, or a combination of both. The scores can be ranked to allow the user to determine the relative environmental concern associated with the chemical, and the manner in which the scores are used is left to the discretion of the user. SCRAM contains a bias toward assigning greater scores for chemicals about which little is known. This bias is intended to drive research to reduce the uncertainty associated with the chemical rather than allowing the chemical to be overlooked. A European system, the EU Risk Ranking Method or EURAM, also uses data availability as one of the criteria for selecting priority substances (HANSEN et al., 1999). The SCRAM chemical scoring and ranking system is designed to expedite an initial screening of large numbers of new and existing chemicals by evaluating a minimal amount of data to identify those chemicals that have greater relative potential to cause problems in the environment. Concentrated effort then may be placed on evaluating more fully those chemicals identified by SCRAM as having a greater likelihood of causing adverse effects due to their toxicity, environmental fate, and uncertainty scores. SCRAM is not meant to serve as a substitute for a risk assessment. Rather, it is intended to lead to risk assessments of chemicals with greater potential for adverse environmental impacts. This system is meant to serve as a tool for managing and prioritizing chemicals for risk assessment and further research. SCRAM has not been developed specifically as a regulatory tool, although it could be used for regulatory activities. SCRAM also could be used prior to large-scale chemical production and use to assess the potential of a chemical to adversely affect organisms in the environment relative to other chemicals already in the environment. It could also be used to decide which of a group of chemicals of potential use for an application is least likely to cause environmental problems. There are probably other potential uses for this system as well.

SCRAM is designed to screen individual chemicals and not to deal with mixtures. Some mixtures of defined composition, such as some pesticide mixtures or Aroclor mixtures, can be screened because environmental monitoring programs are in effect for them, and the individual chemicals in these mixtures occur together in a constant, identifiable ratio. Confounding factors include the limited toxicity database for mixtures and the changing toxic effects due to, for example, differential degradation of mixture components in the environment. Although evaluation of mixtures is important because no organism in the environment is exposed to a single chemical, this system is not equipped to deal with these issues.

2 SCRAM Structure

SCRAM is designed as a flow chart that guides the assessor through the steps of gathering information and assessing the certainty of that information. The spreadsheet is used as a template into which information is incorporated. This information then is aggregated into a composite score. The system is designed to run under release 5.0 or greater of the LOTUS 123[97] spreadsheet program. The system and documentation can be obtained in electronic form from the authors or from the Internet (http://www.epa.gov/toxteam/pbtrept/). SCRAM can be converted for use with other spreadsheet programs, but doing so will result in the loss of many of the labels and masks and is not recommended. The spreadsheet system is depicted graphically in **Fig. 1**-7.

3 Scoring and Aggregation of Scores

3.1 Bioaccumulation

Scoring in SCRAM begins with bioaccumulation and proceeds to persistence *(→ Figs. 1-2)*. Bioaccumulation is scored on the basis of bioaccumulation factors (BAF), bioconcentration factors (BCF), or octanol/water partition coefficients (K_{ow}). A bioaccumulation chemical score is assigned according to the ranges listed in **Fig. 1**, and the score is entered into the appropriate box next to "Chemical Score." The type of information that is available determines an uncertainty

score for bioaccumulation. Measured values for bioaccumulation are given priority over predicted values *(→ Fig. 1)*. If a measured BAF is available, no uncertainty points are assigned. If the value available is a BCF, one uncertainty point is assigned since this would give less information for higher trophic levels where effects of bioaccumulative chemicals are generally greater. If only surrogate information in the form of a K_{ow} is available, 2 uncertainty points are assigned. Finally, if only an estimated BAF or BCF is available, an uncertainty factor of 4 or 5 is assigned, respectively. An estimated BAF or BCF value may be estimated from QSAR based on various properties of the chemical (e.g., K_{ow}, molecular weight, boiling point). The number of uncertainty points for bioaccumulation is entered into the appropriate box next to "Uncertainty Score." The bioaccumulation category is discussed in greater detail in **Part II** of this series (SNYDER et al., 1999a).

3.2 Persistence

Environmental persistence is scored based on ranges of half-lives in five environmental compartments: biota, air, soil, sediment, and water *(→ Fig. 2)*. A score is determined for each compartment, and the greatest score among the five compartments is used as the chemical score for the entire environmental persistence category and entered into the appropriate box next to "Chemical Score." If a measured

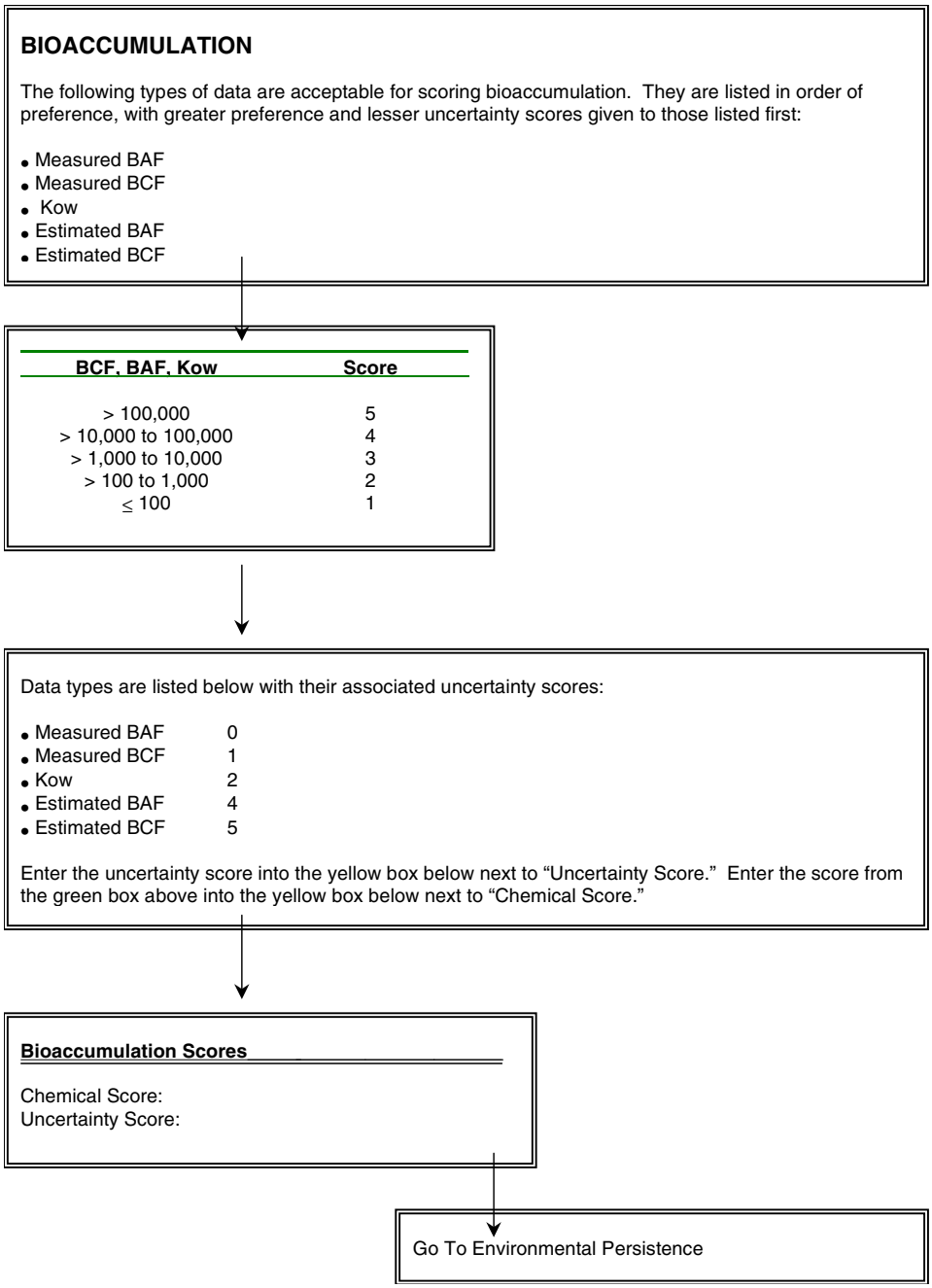
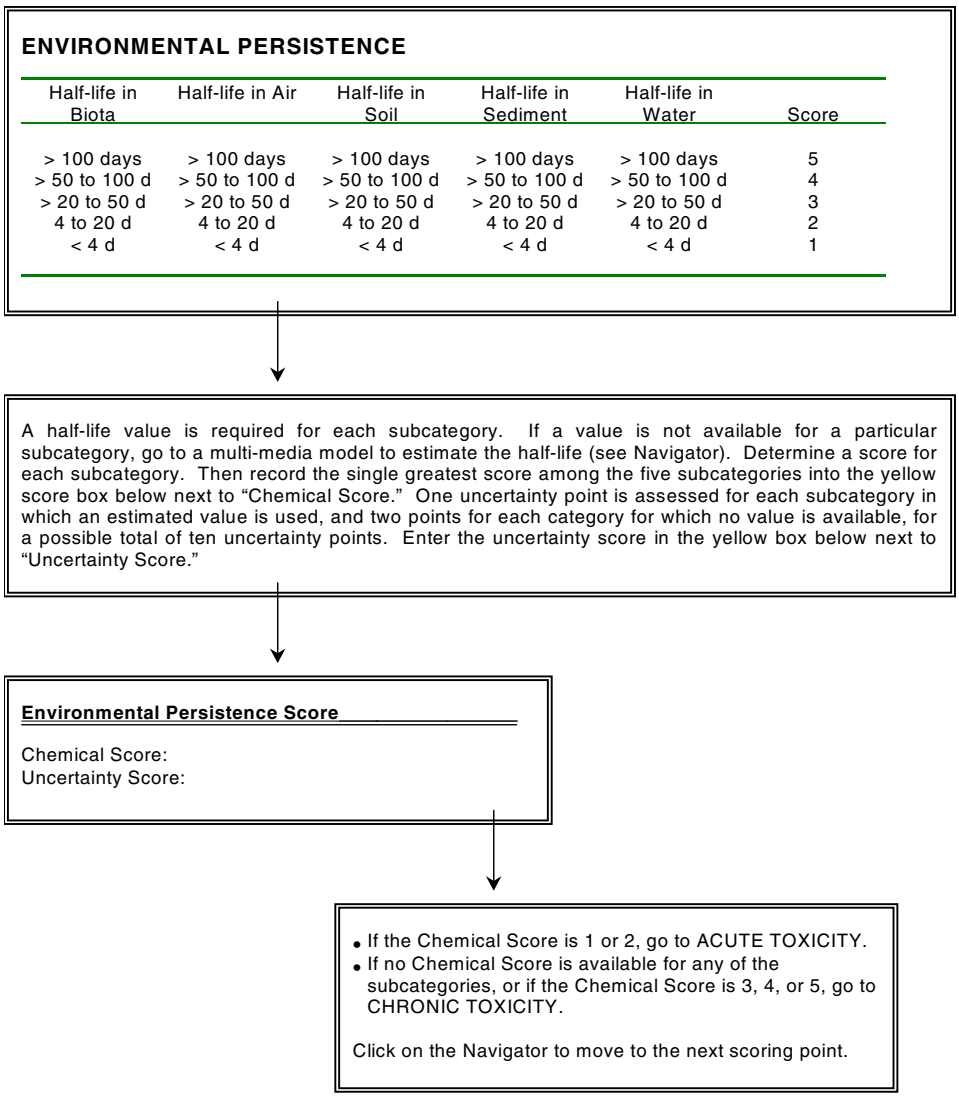


Fig. 1: SCRAM spreadsheet module for scoring bioaccumulation

half-life is not available for a particular compartment, the half-life can be estimated by using a Level III multi-media model (MACKAY, 1991; MACKAY et al., 1996, 1997). The uncertainty associated with environmental persistence is a function of the number of values available for the 5 compartments. One uncertainty point is assigned for each compartment for which an estimated value is used, and two uncertainty points are added for each compartment for which no information is available and no score can be assigned. The total of the uncertainty points for environmental persistence is entered into the appropriate box next to "Uncertainty Score." The persistence category in this scoring and ranking system is described in greater detail in **Part II** of this series (SNYDER et al., 1999a).

Next, the bioaccumulation chemical score (B_{chem}) is multiplied by the persistence chemical score (P_{chem}). These scores are multiplied rather than added for two reasons. First, the multiplication increases the percentage of the final score determined by bioaccumulation and persistence relative to toxicity. Second, bioaccumulation and persistence are the two components that indicate potential for exposure. Multiplying these two scores turns this portion of the system into an exposure index. Exposure is emphasized in the SCRAM scoring system because even if toxic effects are not seen in laboratory toxicity tests, the tests may have failed to result in observed effects for any number of reasons (e.g., mechanisms of action were not identified, effects are very subtle but have long-term consequences). For example, some chemicals are now being shown to cause endocrine disruption effects at levels below those that cause other more overt types of toxicity. However, until recently, little testing was conducted for low-level effects of chemicals on the endocrine system. Exposure is emphasized in the system by, among other approaches, application of a weighting factor to the bioaccumulation and persistence scores.



If the chemical is not persistent, is there continuous environmental loading? If so, go to chronic toxicity.
Does the chemical have metabolite(s) of environmental concern? Score them as well.

Fig.2: SCRAM spreadsheet module for scoring environmental persistence

The product of the persistence and bioaccumulation chemical scores is multiplied by a weighting factor of 1.5 to increase the influence of these properties on the final score.

$$(B_{chem} \times P_{chem})(1.5) \quad (1)$$

The same weighting factor is used for the product of the bioaccumulation and persistence uncertainty scores [Equation 2].

$$(B_{unc} \times P_{unc})(1.5) \quad (2)$$

A factor of 1.5 was chosen because it increases the percentage of the final score associated with bioaccumulation and persistence to an average of greater than 50% (57%) for a list of 21 representative chemicals, placing greater emphasis on exposure, or fate, for scoring relative to toxicity. The list of 21 chemicals and further justification for the weighting factor will be presented in **Part IV** of this series (SNYDER et al., 1999c).

The score for environmental persistence determines which path is taken to score toxicological properties. If the chemical receives a persistence chemical score (P_{chem}) of 1 or 2, the chemical is scored for acute toxicity *(→ Figs. 3-4)*. If the persistence chemical score is 3, 4, or 5, the chemical is scored for subchronic/chronic toxicity *(→ Figs. 5-7, pp. 8-10)*.

3.3 Acute toxicity

The score for acute toxicity is composed of two components; acute aquatic toxicity (AA) and acute terrestrial toxicity (AT). The score for acute terrestrial toxicity is based on toxicity to organisms in five subcategories: plants, mammals, birds, invertebrates, and amphibians and reptiles (herps). Scoring ranges based on ED50 or LD50 values are used to determine a score for each of the five subcategories. The single greatest subcategory value is selected as the chemical score for the acute terrestrial toxicity category and is placed in the appropriate box next to "Chemical Score." An uncertainty point is assigned for each subcategory for which a toxicity value is not available, and the total of the uncertainty points is entered into the appropriate box.

The acute aquatic toxicity score is calculated in a manner analogous to that of the terrestrial section. Each subcategory has a range of scores based on an EC50 or LC50.

ACUTE TERRESTRIAL TOXICITY

PLANTS	MAMMALS	HERPS	BIRDS	INVERTS	
ED50 or LD50 (kg/ha or lb/acre)	Oral ED50 or LD50 (mg/kg/d)	Oral ED50 or LD50 (mg/kg/d)	Oral ED50 or LD50 (mg/kg/d)	ED50 or LD50 (mg/kg)	Score
≤ 0.1	≤ 5	≤ 5	≤ 5	≤ 5	5
> 0.1 to 1	> 5 to 50	> 5 to 50	> 5 to 50	> 5 to 50	4
> 1 to 10	> 50 to 500	> 50 to 500	> 50 to 500	> 50 to 500	3
> 10 to 100	> 500 to 5000	> 500 to 5000	> 500 to 5000	> 500 to 5000	2
> 100	> 5000	> 5000	> 5000	> 5000	1

A toxicity score is required for each subcategory in the green box above. Determine a score for each subcategory, then record the single greatest score among the five subcategories in the yellow score box below next to "Chemical Score." An uncertainty point is assigned for each subcategory for which no toxicity value is available, for a possible total of five uncertainty points. Enter the uncertainty points in the yellow box below, next to "Uncertainty Score."

Acute Terrestrial Toxicity Scores

Chemical Score:
Uncertainty Score:
Composite Score:

Score Acute Aquatic Toxicity

Fig. 3: SCRAM spreadsheet module for scoring acute terrestrial toxicity

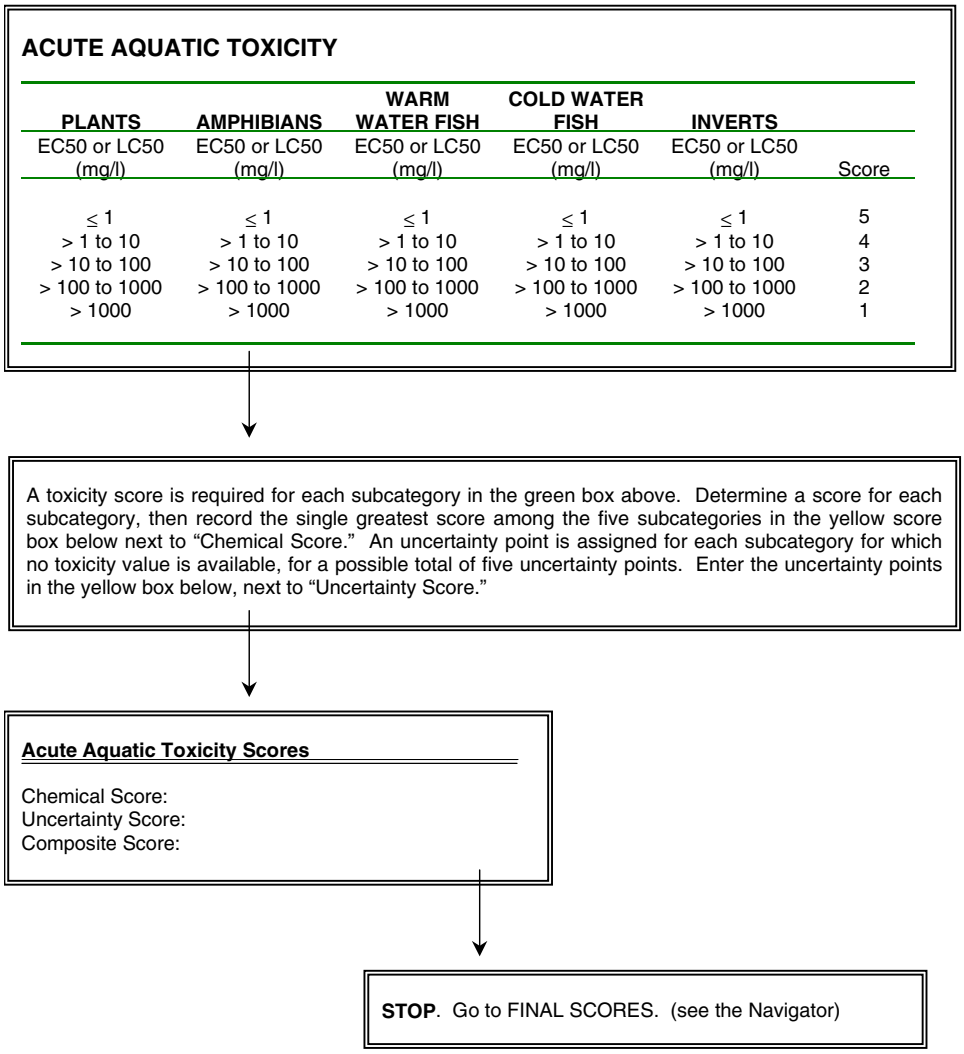


Fig. 4: SCRAM spreadsheet module for scoring acute aquatic toxicity

The greatest score for any of the 5 subcategories (plants, amphibians, warm water fish, cold water fish, invertebrates) is selected as the chemical score for this category. As with the terrestrial section, the uncertainty score is calculated by adding one uncertainty point for each of the subcategories for which no information is available. The acute toxicity category is discussed in greater detail in **Part III** of this series (SNYDER et al., 1999b).

For each of these two acute toxicity categories, the chemical score and the uncertainty score are summed to get the composite score [Equations 3 and 4].

$$AA_{chem} + AA_{unc} = AA_{comp} \quad (3)$$

$$AT_{chem} + AT_{unc} = AT_{comp} \quad (4)$$

These composite scores are calculated so that if the user wishes to determine the basis for the score of a chemical, he or she can quickly look over the bioaccumulation, persistence, and toxicity score boxes in the SCRAM system to determine the relative contribution of toxicity to the final score. The chemical score for each category is added to the product of the bioaccumulation and persistence chemical scores and the weighting factor of 1.5 to determine the final chemical score [F_{chem}; Equation 5].

$$F_{chem} = (B_{chem} \times P_{chem})(1.5) + AA_{chem} + AT_{chem} \quad (5)$$

To determine the final uncertainty score for the acute toxicity pathway (F_{unc}) the product of the bioaccumulation and persistence uncertainty scores and the weighting factor of 1.5 is added to the uncertainty scores from the acute aquatic toxicity and acute terrestrial toxicity categories [Equation 6].

$$F_{unc} = (B_{unc} \times P_{unc})(1.5) + AA_{unc} + AT_{unc} \quad (6)$$

3.4 Subchronic/Chronic toxicity

If the subchronic/chronic toxicity path is taken, there are three toxicity categories to consider: subchronic/chronic terrestrial toxicity (CT), subchronic/chronic aquatic toxicity (CA), and subchronic/chronic human toxicity (CH). The

SUBCHRONIC/CHRONIC TERRESTRIAL TOXICITY*

PLANTS	MAMMALS		HERPS		BIRDS		INVERTS	
LO(A)EL or NO(A)EL (kg/ha or lb/acre)	LO(A)EL (mg/kg/d)	≥ 90d NO(A)EL (mg/kg/d)	LO(A)EL (mg/kg/d)	≥ 90d NO(A)EL (mg/kg/d)	LO(A)EL (mg/kg/d)	≥ 90d NO(A)EL (mg/kg/d)	LO(A)EL or NO(A)EL (mg/kg)	Score
≤ 0.1	≤ 10	≤ 1	≤ 10	≤ 1	≤ 10	≤ 1	≤ 10	5
> 0.1 to 1	> 10 to 100	> 1 to 10	> 10 to 100	> 1 to 10	> 10 to 100	> 1 to 10	> 10 to 100	4
> 1 to 10	> 100 to 1000	> 10 to 100	> 100 to 1000	> 10 to 100	> 100 to 1000	> 10 to 100	> 100 to 1000	3
> 10 to 100	> 1000 to 5000	> 100 to 1000	> 1000 to 5000	> 100 to 1000	> 1000 to 5000	> 100 to 1000	> 1000 to 5000	2
> 100	> 5000	> 1000	> 5000	> 1000	> 5000	> 1000	> 5000	1

A toxicity score is required for each subcategory in the green box above. Determine a score for each subcategory, then record the single greatest score among the five subcategories in the yellow score box below next to "Chemical Score." An uncertainty point is assigned for each subcategory for which no toxicity value is available, for a possible total of five uncertainty points. Enter the uncertainty points in the yellow box below, next to "Uncertainty Score."

All terrestrial chronic toxicity LO(A)EL values should be corrected with a severity factor. Multiply the LO(A)EL (mg/kg/d) by 0.1 for severe effects or by 0.3 for moderate effects, then score the chemical using the corrected LO(A)EL. Where a LO(A)EL and NO(A)EL are both available from the same study, the NO(A)EL is preferred. If, from a separate study, a LO(A)EL is found that is lower than the lowest NO(A)EL, the LO(A)EL is preferred.

Chronic Terrestrial Toxicity Scores

Chemical Score:
Uncertainty Score:
Composite Score:

Score Subchronic/Chronic Aquatic Toxicity

***NOTE**: When studies of ≥ 90 days are not available, repeated dose studies of lesser duration (≥ 28d) may be used. For these shorter term studies, a safety factor of 3 should be applied to the criteria dosage level unless data indicate that steady state conditions (equilibrium) have been reached and the expected critical effect has been adequately evaluated from less than 90d exposures.

Fig. 5: SCRAM spreadsheet module for scoring subchronic/chronic terrestrial toxicity

score for subchronic/chronic terrestrial toxicity is based on toxicity to organisms in five subcategories: plants, mammals, birds, invertebrates, and amphibians and reptiles (herps). Scores are based on the no observed adverse effect level (NOAEL), no observed effect level (NOEL), lowest observed adverse effect level (LOAEL), or lowest observed effect level (LOEL). [Note: Hereafter, "NO(A)EL" means either NOEL or NOAEL, and "LO(A)EL" means either LOEL or LOAEL.] A score is generated for each of the 5 subcategories. The single greatest subcategory score is selected as the chemical score for the subchronic/chronic terrestrial toxicity category and is placed in the appropriate box next to "Chemical Score." An uncertainty point is assigned for each subcategory for which a value is not available.

The subchronic/chronic aquatic toxicity score *(→ Fig. 6, p. 9)* is calculated in a manner analogous to that of the acute terrestrial toxicity category. Each subcategory has a range of scores based on the no observed adverse effect concentration (NOAEC), no observed effect concentration (NOEC), lowest observed adverse effect concentration (LOAEC), lowest observed effect concentration (LOEC), or maximum acceptable toxicant concentration (MATC). [Note: Hereafter, "NO(A)EC" means NOAEC or NOEC, and "LO(A)EC" means LOAEC or LOEC.] The greatest score for any of the five subcategories (plants, amphibians, warm water fish, cold water fish, invertebrates) is selected as the chemical score for this category. As with the acute terrestrial toxicity category, the uncertainty score is calculated by adding one uncertainty point for each of the subcategories for which no information is available.

The subchronic/chronic human toxicity category is divided into five subcategories: general toxicity, reproductive toxicity, developmental toxicity, carcinogenicity, and "other toxicity." All of these subcategories are scored on the basis of NO(A)EL or LO(A)EL values except for carcinogenicity, which is scored on the basis of an ED10 value (effect dose 10). A score is determined for each subcategory, and the single greatest score among the subcategories is selected as the chemical score for the category. An uncertainty point is assigned for each subcategory for which there is no toxicity value, with the exception of the "other toxicity" category. The subchronic/chronic toxicity category is described in greater detail in **Part III** of this series (SNYDER et al., 1999b).

For each of these three subchronic/chronic toxicity categories, the chemical score and the uncertainty score are summed to get the composite score [Equations 7-9].

$$CA_{chem} + CA_{unc} = CA_{comp} \quad (7)$$

$$CT_{chem} + CT_{unc} = CT_{comp} \quad (8)$$

$$CH_{chem} + CH_{unc} = CH_{comp} \quad (9)$$

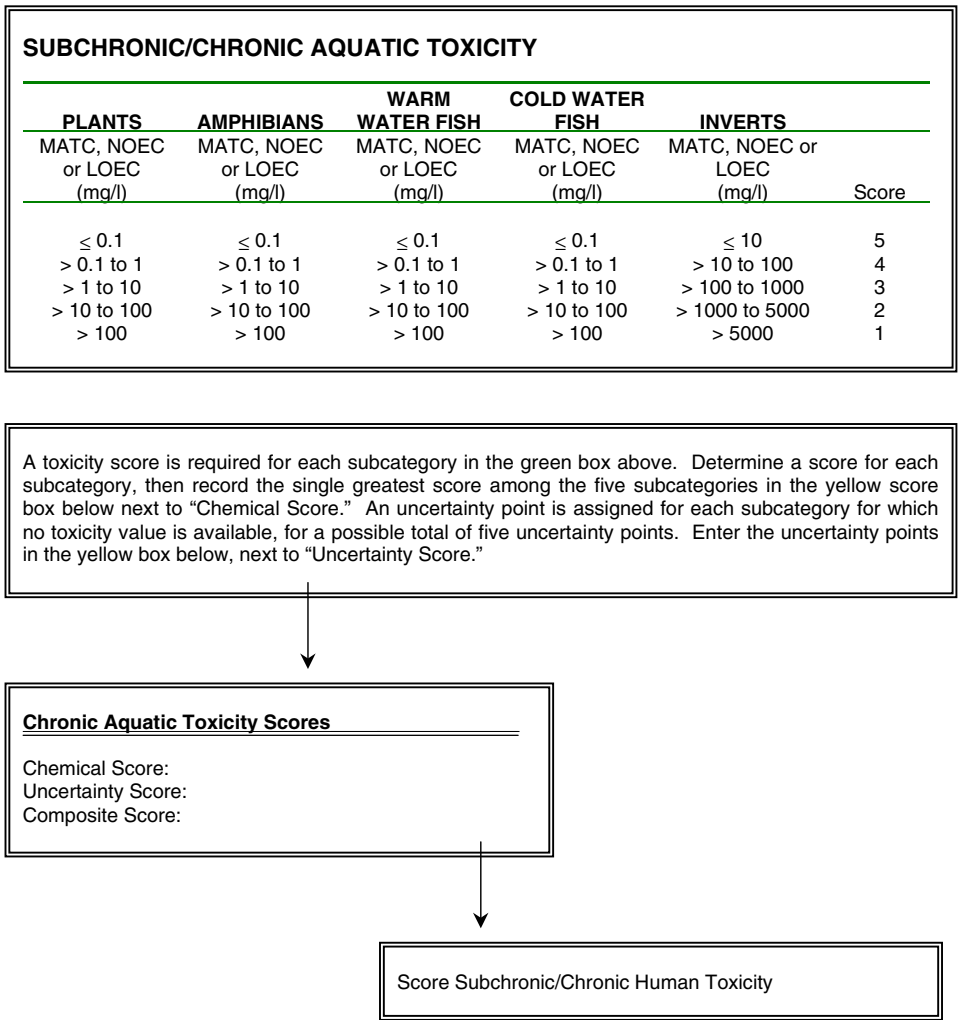


Fig. 6: SCRAM spreadsheet module for scoring subchronic/chronic aquatic toxicity

The chemical score for each category is added to the product of the bioaccumulation and persistence chemical scores and the weighting factor of 1.5 to determine the final chemical score [F_{chem}; Equation 10].

$$F_{chem} = (B_{chem} \times P_{chem})(1.5) + CA_{chem} + CT_{chem} + CH_{chem} \quad (10)$$

The final uncertainty score for the subchronic/chronic pathway (F_{unc}) is calculated in a manner analogous to that for the acute pathway [Equation 11].

$$F_{unc} = (B_{unc} \times P_{unc})(1.5) + CA_{unc} + CT_{unc} + CH_{unc} \quad (11)$$

3.5 Final composite score

Regardless of whether the subchronic/chronic or acute path is taken, the final composite score is calculated as the sum of the final chemical score and the final uncertainty score [Equation 12].

$$F_{comp} = F_{chem} + F_{unc} \quad (12)$$

For maximum chemical scores and uncertainty scores for each scoring category in SCRAM, see **Table 1**. Some conventions followed in scoring chemicals are as follows. 1) When reporting scores, round to the next greater integer. 2) When the uncertainty score is zero for persistence or bioaccumulation, but not both, the system converts the zero to a one for the purpose of multiplication so that the uncertainty points for the other category are not canceled out.

Table 1: Maximum chemical and uncertainty scores for SCRAM scoring categories

Scoring Category	Maximum Chemical Score	Maximum Uncertainty Score
Bioaccumulation	5	5
Persistence	5	10
Acute Terrestrial Toxicity	5	5
Acute Aquatic Toxicity	5	5
Subchronic/Chronic Terrestrial Toxicity	5	5
Subchronic/Chronic Aquatic Toxicity	5	5
Subchronic/Chronic Human Toxicity	5	4

Includes human epidemiological data and established rodent and simian test protocols data. All other test data will be scored under chronic/subchronic terrestrial toxicity. All LO(A)EL values should be corrected with a severity factor. Multiply the LO(A)EL (mg/kg/d) by 0.1 for severe effects or by 0.3 for moderate effects. Then score the chemical by using the corrected LO(A)EL. Where LO(A)EL and NO(A)EL are both available from the same study, the NO(A)EL is preferred. If, from a separate study, a LO(A)EL is found that is lower than the lowest NO(A)EL, the LO(A)EL is preferred.

*NOTE: If studies of ≥ 90days are not available, see note in subchronic/chronic terrestrial toxicity. For human toxicity, the user may elect to follow the convention described in the Ontario MOEE Scoring System as follows:
⇨ 28-89d, multiply the criteria dosage levels by a factor of 0.1
⇨ repeated doses < 28d, multiply the criteria dosage levels by 0.01

SUBCHRONIC/CHRONIC HUMAN TOXICITY*

General Toxicity**		Reproductive Toxicity		Developmental Toxicity		Carcinogenicity (See ***)	Other Toxicity (See ****)	
LO(A)EL (mg/kg/d)	NO(A)EL (mg/kg/d)	LO(A)EL (mg/kg/d)	NO(A)EL (mg/kg/d)	LO(A)EL (mg/kg/d)	NO(A)EL (mg/kg/d)	See calculation box (mg/kg/d)	See calculation box (mg/kg/d)	Score
≤ 10	≤ 1	≤ 10	≤ 1	≤ 10	≤ 1	> 45		5
> 10 to 100	> 1 to 10	> 10 to 100	> 1 to 10	> 10 to 100	> 1 to 10	> 15 to 45		4
> 100 to 1000	> 10 to 100	> 100 to 1000	> 10 to 100	> 100 to 1000	> 10 to 100	> 5 to 15		3
> 1000 to 5000	> 100 to 1000	> 1000 to 5000	> 100 to 1000	> 1000 to 5000	> 100 to 1000	> 1.5 to 5		2
> 5000	> 1000	> 5000	> 1000	> 5000	> 1000	≤ 1.5		1

A toxicity score is required for each subcategory in the green box above. Determine a score for each subcategory, then record the single greatest score among the five subcategories in the yellow score box below next to "Chemical Score." An uncertainty point is assigned for each subcategory for which no toxicity value is available, for a possible total of five uncertainty points. Enter the uncertainty points in the yellow box below, next to "Uncertainty Score."

CARCINOGENICITY CALCULATIONS BOX
*** For the carcinogenicity category, multiply the 1/ED10 value by a weight of evidence factor (USEPA classification).

- "Known human carcinogen" = 3
- "Likely human carcinogen" = 2
- "Suggestive evidence of carcinogenicity" or "Conflicting Data" = 1

Then use the corrected value to score the chemical.

1/ED10 (mg/kg/d)	Score Values
> 45	5
> 15 to 45	4
> 5 to 15	3
> 1.5 to 5	2
≤ 1.5	1

Return to CHRONIC HUMAN TOXICITY. (see the Navigator)

Fig. 7a: SCRAM spreadsheet module for scoring subchronic/chronic human toxicity

SUBCHRONIC/CHRONIC HUMAN TOXICITY (continued)…
* EXPOSURE DURATION: When studies of ≥ 90d are not available, repeated-dose studies of lesser duration (≥ 28d) may be used. For these shorter term studies, criteria dosage levels for scoring should be decreased by a factor of 3 unless data indicate that steady state test conditions (equilibrium) have been reached and the expected critical effect may be adequately evaluated from less than 90d exposures.

** GENERAL TOXICITY: General organ system toxicity, i.e. hepatotoxicity, neurotoxicity, renal toxicity, etc…

****OTHER TOXICITY: Effects such as mutagenicity, immunotoxicity, endocrine system effects, etc. Where well-established test protocols may be lacking, where the level of test data is minimal, where whole animal test data are not readily available and predictive in vitro-type assay data must be considered in lieu of whole animal assays. Scores may be assigned based on narrative definition or description. See the sample calculation box below.

NOTE: Lack of data in the "OTHER TOXICITY" category will NOT generate an uncertainty score for the subcategory. Instead, the subcategory acts as a modifier to the total toxicity score.

****OTHER TOXICITY:**

MUTAGENICITY	BEHAVIORAL EFFECTS	IMMUNE SYS. EFFECTS	ENDOCRINE EFFECTS	Score
Positive germ line	Severe-Irreversible	Severe-Irreversible	---	5
Possible germ line	Severe-Reversible or Moderate-Irreversible	Severe-Reversible or Moderate-Irreversible	---	4
Positive somatic line	Moderate-Reversible	Moderate-Reversible	High potential	3
Possible somatic line	Slight effects	Slight effects	Moderate potential	2
No known mutagenic effects	No known effects	No known effects	Low potential	1

Chronic Human Toxicity Scores
Chemical Score:
Uncertainty Score:
Composite Score:

Total Chronic Toxicity Scores
Chemical Score:
Uncertainty Score:
Composite Score:

STOP. Go to FINAL SCORES (See the Navigator)

Total Chronic Toxicity = Chronic Terrestrial Toxicity + Chronic Aquatic Toxicity + Chronic Human Toxicity

FINAL SCORES
Chemical Score:
Uncertainty Score:
Composite Score:

Fig. 7b: SCRAM spreadsheet module for scoring subchronic/chronic human toxicity (continued)

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